Figure 1 – Starting sequence used for the codon modification of MUC1. The MUC1 expression cassette sequence is taken from the vector JNW656. Start and stop codons are bolded. Kozak sequence is italicised. Restriction sites are underlined.

GCTAGC*GCCACC***ATG**TCTAGAACACCGGGCACCCAGTCTCCTTTCTTCCTGCT
GCTGCTCCTCACAGTGCTTACAGTTGTTACAGGTTCTGGTCATGCAAGCTCTAC
CCCAGGTGGAGAAAAGGAGACTTCGGCTACCCAGAGAAGTTCAGTGCCCAGCT
CTACTGAGAAGAATGCTGTGAGTATGACCAGCAGCGTACTCTCCAGCCACAGcC
CCGGTTCAGGCTCCTCCACCACTCAGGGACAGGATGTCACTCTGGCCCCGGCC
ACGGAACCAGCTTCAGGTTCAGCTGCCACCTGGGGACAGGATGTCACCTCGGT
CCCAGTCACCAGGCCAGCCCTGGGCTCCACCACCCCGCCAGCCCACGATGTC
ACCTCAGCCCCGGACAACAAGCCAGCCCCGGGCTCCACCGCCCCCCCAGCCC
ACGGTGTCACCTCGGCCCCGGACACCAGGCCGGCCCCGGGCTCCACCGCCCC
CCCAGCCCACGGTGTCACCTCGGCCCCGGACACCAGGCCGGCCCCGGGCTCC
ACCGCCCCCCCAGCCCACGGTGTCACCTCGGCCCCGGACACCAGGCCGGCCC
CGGGCTCCACCGCCCCCCCAGCCCACGGTGTCACCTCGGCCCCGGACACCAG
GCCCGCCCCGGGCTCCACCGCCCCCCCAGCCCACGGTGTCACCTCGGCCCCG
GACACCAGGCCCGCCCCGGGCTCCACCGCGCCCGCAGCCCACGGTGTCACCT
CGGCCCCGGACACCAGGCCGGCCCCGGGCTCCACCGCCCCCCCAAGCCCACG
GTGTCACCTCGGCCCCGGACACCAGGCCGGCCCCGGGCTCCACCGCCCCCCC
AGCCCATGGTGTCACCTCGGCCCCGGACAACAGGCCCCGCCTTGGGCTCCACC
GCCCCTCCAGTCCACAATGTCACCTCGGCCTCAGGCTCTGCATCAGGCTCAGC
TTCTACTCTGGTGCACAACGGCACCTCTGCCAGGGCTACCACAACCCCAGCCA
GCAAGAGCACTCCATTCTCAATTCCCAGCCACCACTCTGATACTCCTACCACCC
TTGCCAGCCATAGCACCAAGACTGATGCCAGTAGCACTCACCATAGCACGGTA
CCTCCTCTCACCTCCTCCAATCACAGCACTTCTCCCCAGTTGTCTACTGGGGTC
TCTTTCTTTTTCCTGTCTTTTCACATTTCAAACCTCCAGTTTAATTCCTCTCTGGA
AGATCCCAGCACCGACTACTACCAAGAGCTGCAGAGAGACATTTCTGAAATGTT
TTTGCAGATTTATAAACAAGGGGGTTTTCTGGGCCTCTCCAATATTAAGTTCAG
GCCAGGATCTGTGGTGGTACAATTGACTCTGGCCTTCCGAGAAGGTACCATCA
ATGTCCACGACGTGGAGACACAGTTCAATCAGTATAAAACGGAAGCAGCCTCTC
GATATAACCTGACGATCTCAGACGTCAGCGTGAGTGATGTGCCATTTCCTTTCT
CTGCCCAGTCTGGGGCTGGGGTGCCAGGCTGGGGCATCGCGCTGCTGGTGCT
GGTCTGTGTTCTGGTTGCGCTGGCCATTGTCTATCTCATTGCCTTGGCTGTCTG
TCAGTGCCGCCGAAAGAACTACGGGCAGCTGGACATCTTTCCAGCCCGGGATA
CCTACCATCCTATGAGCGAGTACCCCACCTACCACACCCATGGGCGCTATGTG
CCCCCTAGCAGTACCGATCGTAGCCCCTATGAGAAGGTTTCTGCAGGTAATGG
TGGCAGCAGCCTCTCTTACACAAACCCAGCAGTGGCAGCCACTTCTGCCAACTT
GTCTAGA**TAG**CTCGAG

Figure 2 – MUC1 sequence devoid of the 7x VNTR repeat sequence, prior to codon modification. The start and stop codons are bolded. Restriction cloning sites are underlined. The BlpI and BbvCI sites for insertion of the 7x VNTR fragment are double underlined.

ATGTCTAGAACACCGGGCACCCAGTCTCCTTTCTTCCTGCTGCTGCTCCTCACA
GTGCTTACAGTTGTTACAGGTTCTGGTCATGCAAGCTCTACCCCAGGTGGAGAA
AAGGAGACTTCGGCTACCCAGAGAAGTTCAGTGCCCAGCTCTACTGAGAAGAA
TGCTGTGAGTATGACCAGCAGCGTACTCTCCAGCCACAGCCCCGGTTCAGGCT
CCTCCACCACTCAGGGACAGGATGTCACTCTGGCCCCGGCCACGGAACCAGCT
TCAGGTTCAGCTGCCACCTGGGGACAGGATGTCACCTCGGTCCCAGTCACCAG
GCCAGCCCTGGGCTCCACCACCCCGCCAGCCCACGATGTCACCTCAGCCCCG
GACAACAAGCCCAATGTCACCTCGGCCTCAGGCTCTGCATCAGGCTCAGCTTC
TACTCTGGTGCACAACGGCACCTCTGCCAGGGCTACCACAACCCCAGCCAGCA
AGAGCACTCCATTCTCAATTCCCAGCCACCACTCTGATACTCCTACCACCCTTG
CCAGCCATAGCACCAAGACTGATGCCAGTAGCACTCACCATAGCACGGTACCT
CCTCTCACCTCCTCCAATCACAGCACTTCTCCCCAGTTGTCTACTGGGGTCTCT
TTCTTTTTCCTGTCTTTTCACATTTCAAACCTCCAGTTTAATTCCTCTCTGGAAGA
TCCCAGCACCGACTACTACCAAGAGCTGCAGAGAGACATTTCTGAAATGTTTTT
GCAGATTTATAAACAAGGGGGTTTTCTGGGCCTCTCCAATATTAAGTTCAGGCC
AGGATCTGTGGTGGTACAATTGACTCTGGCCTTCCGAGAAGGTACCATCAATGT
CCACGACGTGGAGACACAGTTCAATCAGTATAAAACGGAAGCAGCCTCTCGATA
TAACCTGACGATCTCAGACGTCAGCGTGAGTGATGTGCCATTTCCTTTCTCTGC
CCAGTCTGGGGCTGGGGTGCCAGGCTGGGGCATCGCGCTGCTGGTGCTGGTC
TGTGTTCTGGTTGCGCTGGCCATTGTCTATCTCATTGCCTTGGCTGTCTGTCAG
TGCCGCCGAAAGAACTACGGGCAGCTGGACATCTTTCCAGCCCGGGATACCTA
CCATCCTATGAGCGAGTACCCCACCTACCACACCCATGGGCGCTATGTGCCCC
CTAGCAGTACCGATCGTAGCCCCTATGAGAAGGTTTCTGCAGGTAATGGTGGC
AGCAGCCTCTCTTACACAAACCCAGCAGTGGCAGCCACTTCTGCCAACTTGTCT
AGA**TAG**

Figure 3 – Two representative MUC1 codon modified sequences

Sequence 1

ATGAGCCGGACCCCTGGCACCCAGTCTCCATTCTTCCTGCTCCTGCTGCTCAC
CGTGCTGACCGTGGTGACGGGAAGCGGCCACGCTTCGTCCACGCCCGGCGGC
GAGAAGGAAACCAGTGCAACCCAGCGCAGCTCCGTGCCCAGCTCCACCGAGA
AAAACGCTGTGAGCATGACGTCCAGTGTCCTCTCTAGCCATAGCCCCGGCTCT
GGGAGCAGTACCACCCAGGGCCAGGACGTGACTCTCGCCCCCGCTACGGAGC
CCGCTTCTGGCTCCGCCGCCACCTGGGGCCAGGACGTGACCTCTGTGCCGGT
CACACGCCCTGCTCTGGGCTCTACCACTCCTCCTGCCCATGACGTGACCTCGG
CTCCGGACAATAAGCCCAACGTGACGAGTGCCAGCGGGAGCGCCTCGGGGTC
CGCCAGTACCCTGGTGCATAACGGGACCAGTGCTAGGGCCACCACCACCCCC
GCGTCGAAGAGCACCCCCTTCTCTATCCCGTCTCATCATAGCGACACACCTACA
ACCCTGGCGAGCCACAGCACCAAGACCGACGCTTCTTCCACACATCATAGCAC
CGTGCCACCACTCACCAGCTCCAACCATTCCACCAGCCCCCAGCTGAGCACCG
GAGTGTCCTTCTTCTTCCTGAGCTTCCATATCAGTAACCTCCAGTTCAACTCCAG
CCTCGAGGACCCCTCTACCGACTACTATCAGGAGCTGCAGCGGGACATCAGCG
AGATGTTTCTGCAGATCTACAAGCAGGGGGGCTTCCTCGGCCTGTCTAACATCA
AGTTCCGCCCCGGCAGCGTCGTGGTGCAGTTGACCCTGGCCTTCCGGGAGGG
CACCATCAACGTGCACGACGTGGAGACCCAGTTCAACCAGTACAAGACCGAGG
CCGCCAGCAGGTATAACCTGACCATCTCCGACGTCTCTGTGAGCGACGTCCCC
TTCCCTTTCTCCGCCCAGAGCGGCGCTGGGGTGCCCGGCTGGGGCATCGCCT
TGCTCGTGCTGGTGTGCGTGCTGGTGGCCCTGGCCATCGTGTACCTGATCGCC
CTGGCCGTCTGTCAATGCAGGCGCAAGAACTACGGCCAGCTCGACATCTTCCC
AGCTCGGGATACCTATCATCCCATGAGCGAGTACCCCACCTACCACACCCATG
GCCGCTACGTTCCTCCCTCCAGCACCGACCGCAGCCCTTACGAGAAGGTGAGC
GCCGGGAATGGGGGGAGTTCTCTCTCTTACACAAACCCCGCCGTGGCCGCCA
CGAGCGCCAACCTCTCCAGGTGA

Sequence 2

ATGTCCCGCACCCCTGGCACCCAGTCCCCCTTCTTTCTCCTGCTGCTGCTCACC
GTGCTGACCGTCGTGACCGGCAGTGGGCATGCGTCCTCGACGCCCGGCGGCG
AGAAGGAGACCAGTGCTACCCAGCGCAGCTCTGTGCCTTCCAGCACGGAGAAG
AACGCTGTGAGTATGACTTCCTCCGTGCTGAGCTCCCATAGCCCCGGCTCGGG
CAGCTCCACCACCCAGGGGCAGGACGTGACACTGGCTCCCGCAACCGAGCCC
GCCTCTGGCTCTGCCGCCACCTGGGGCCAGGACGTGACATCCGTGCCCGTGA
CCCGCCCCGCCCTGGGCAGCACCACCCCCCCTGCTCATGACGTCACCTCTGC
GCCTCCACACTGGTGCATAACGGAACCTCCGCGCGCGCCACCACCACCCCAG
CGAGCAAGAGCACCCCCTTCTCTATCCCCTCCCATCATAGCGACACACCCACCA
CGCTGGCCAGCCATAGCACCAAAACCGACGCCTCTAGCACCCACCACTCCACG
GTGCCCCCCCCTGACCTCCAGCAACCATTCTACCTCCCCCCAGCTGAGCACGGG
GGTGAGCTTTTTCTTCCTGTCCTTCCATATCAGCAACCTCCAGTTCAATTCCTCT
CTGGAGGACCCCAGCACCGACTACTACCAAGAGCTGCAGCGGGACATCTCCGA
GATGTTCCTGCAGATCTACAAACAGGGCGGCTTCTTGGGATTGAGCAACATCAA
GTTCCGCCCCGGGTCCGTGGTGGTGCAGCTCACCCTGGCCTTCAGGGAGGGC
ACCATCAACGTGCATGACGTCGAGACCCAGTTCAATCAGTATAAGACCGAGGC
CGCCTCCCGGTACAACCTGACGATCAGCGACGTGTCTGTGTCCGACGTGCCCT
TCCCCTTCTCCGCACAGTCCGGCGCCGGCGTGCCGGGCTGGGGCATCGCCCT

GCTCGTGTTGGTGTGCGTGCTCGTGGCCCTCGCCATCGTGTACCTGATCGCCC
TGGCCGTCTGTCAGTGCAGGAGAAAGAACTATGGGCAGTTGGATATCTTCCCC
GCCAGGGACACCTACCACCCCATGTCCGAGTACCCCACCTACCACACCCACGG
CCGCTATGTCCCTCCCTCCTCGACCGACCGCTCCCCTTACGAGAAGGTGAGCG
CCGGCAACGGAGGCAGCTCCCTGTCCTACACCAACCCTGCCGTGGCCGCCAC
AAGCGCCAACCTGAGCCGCTGA

Figure 4 – Engineered MUC1 codon modified sequence including restriction sites (underlined), Kozak sequence (italicised), start and stop codons (bolded), BbvCI (boxed) and BlpI (boxed). The later two features are essential for the re-introduction of the 7x VNTR fragment.

GCAGGCGGCCGCGCTAGC*GCCACC***ATG**TCTAGAACCCCTGGCACCCAGTCCC
CCTTCTTTCTCCTGCTGCTGCTCACCGTGCTGACCGTCGTGACCGGCAGTGGG
CATGCGTCCTCGACGCCCGGCGGCGAGAAGGAGACCAGTGCTACCCAGCGCA
GCTCTGTGCCTTCCAGCACGGAGAAGAACGCTGTGAGTATGACTTCCTCCGTG
CTGTCCTCCCATAGCCCCGGCTCGGGCAGCTCCACCACCCAGGGGCAGGACG
TGACACTGGCTCCCGCAACCGAGCCCGCCTCTGGCTCTGCCGCCACCTGGGG
CCAGGACGTGACATCCGTGCCCGTGACCCGCCCCGCCCTGGGCAGCACCACC
CCCCCTGCTCATGACGTCACCTCAGCGCCTGACAACAAGCCTAACGTGACGTC
CGCTTCCGGCAGCGCCTCCGGCTCAGCCTCCACACTGGTGCATAACGGAACCT
CCGCGCGCGCCACCACCACCCCAGCGAGCAAGAGCACCCCCTTCTCTATCCCC
TCCCATCATAGCGACACACCCACCACGCTGGCCAGCCATAGCACCAAAACCGA
CGCCTCTAGCACCCACCACTCCACGGTGCCCCCCCTGACCTCCAGCAACCATT
CTACCTCCCCCCAGCTGTCCACGGGGGTGAGCTTTTTCTTCCTGTCCTTCCATA
TCAGCAACCTCCAGTTCAATTCCTCTCTGGAGGACCCCAGCACCGACTACTACC
AAGAGCTGCAGCGGGACATCTCCGAGATGTTCCTGCAGATCTACAAACAGGGC
GGCTTCCTGGGATTGAGCAACATCAAGTTCCGCCCCGGGTCCGTGGTGGTGCA
GCTCACCCTGGCCTTCAGGGAGGGCACCATCAACGTGCATGACGTCGAGACCC
AGTTCAATCAGTATAAGACCGAGGCCGCCTCCCGGTACAACCTGACGATCAGC
GACGTGTCTGTGTCCGACGTGCCCTTCCCCTTCTCCGCACAGTCCGGCGCCGG
CGTGCCGGGCTGGGGCATCGCCCTGCTCGTGTTGGTGTGCGTGCTCGTGGCC
CTCGCCATCGTGTACCTGATCGCCCTGGCCGTCTGTCAGTGCAGGAGAAAGAA
CTATGGGCAGTTGGATATCTTCCCCGCCAGGGACACCTACCACCCCATGTCCG
AGTACCCCACCTACCACACCCACGGCCGCTATGTCCCTCCCTCCTCGACCGAC
CGCTCCCCTTACGAGAAGGTGAGCGCCGGCAACGGAGGCAGCTCCCTGTCCT
ACACCAACCCTGCCGTGGCCGCCACAAGCGCCAACCTGTCTAGA**TGA**CTCGAG
GGATCCGCAG

Figure 5 – Final codon modified sequence of the MUC1 expression cassette containing the 7x VNTR fragment from JNW758. This cassette has a codon coefficient index of 0.699. Restriction sites are underlined, start and stop codons are bolded, the Kozak sequence is italicised, the BbvCI and BlpI sites are boxed, and the positions of the two silent mutations are double underlined.

GCTAGC*GCCACC***ATG**TCTAGAACCCCTGGCACCCAGTCCCCCTTCTTTCTCCTG
CTGCTGCTCACCGTGCTGACCGTCGTGACCGGCAGTGGGCATGCGTCCTCGA
CGCCCGGCGGCGAGAAGGAGACCAGTGCTACCCAGCGCAGCTCTGTGCCTTC
CAGCACGGAGAAGAACGCTGTGAGTATGACTTCCTCCGTGCTGTCCTCCCATA
GCCCCGGCTCGGGCAGCTCCACCACCCAGGGGCAGGACGTGACACTGGCTCC
CGCAACCGAGCCCGCCTCTGGCTCTGCCGCCACCTGGGGCCAGGACGTGACA
TCCGTGCCCGTGACCCGCCCCGCCCTGGGCAGCACCACCCCCCCTGCTCATG
ACGTCACCTCAGCCCCGGACAACAAGCCAGCCCCGGGCTCCACCGCCCCCCC
AGCCCACGGTGTCACCTCGGCCCCGGACACCAGGCCGGCCCCGGGCTCCACC
GCCCCCCCAGCCCACGGTGTCACCTCGGCCCCGGACACCAGGCCGGCCCCG
GGCTCCACCGCCCCCCCAGCCCACGGTGTCACCTCGGCCCCGGACACCAGGC
CGGCCCCGGGCTCCACCGCCCCCCCAGCCCACGGTGTCACCTCGGCCCCGGA
CACCAGGCCCGCCCCGGGCTCCACCGCCCCCCCAGCCCACGGTGTCACCTCG
GCCCCGGACACCAGGCCCGCCCCGGGCTCCACCGCGCCCGCAGCCCACGGT
GTCACCTCGGCCCCGGACACCAGGCCGGCCCCGGGCTCCACCGCCCCCCAAG
CCCACGGTGTCACCTCGGCCCCGGACACCAGGCCGGCCCCGGGCTCCACCGC
CCCCCCAGCCCATGGTGTCACCTCGGCCCCGGACAACAGGCCCGCCTTGGGC
TCCACCGCCCCTCCAGTCCACAATGTCACCTCGGCCTCAGGCTCTGCATCAGG
CTCAGCCTCCACACTGGTGCATAACGGAACCTCCGCGCGCGCCACCACCACCC
CAGCGAGCAAGAGCACCCCCTTCTCTATCCCCTCCCATCATAGCGACACACCC
ACCACGCTGGCCAGCCATAGCACCAAAACCGACGCCTCTAGCACCCACCACTC
CACGGTGCCCCCCCCTGACCTCCAGCAACCATTCTACCTCCCCCCAGCTGTCCA
CGGGGGTGAGCTTTTTCTTCCTGTCCTTCCATATCAGCAACCTCCAGTTCAATT
CCTCTCTGGAGGACCCCAGCACCGACTACTACCAAGAGTTGCAGCGGGACATC
TCCGAGATGTTCCTGCAGATCTACAAACAGGGCGGCTTCCTGGGATTGAGCAA
CATCAAGTTCCGCCCCGGGTCCGTGGTGGTGCAGCTCACCCTGGCCTTCAGG
GAGGGCACCATCAACGTGCATGACGTCGAGACCCAGTTCAATCAGTATAAGAC
CGAGGCCGCCTCCCGGTACAACCTGACGATCAGCGACGTGTCTGTGTCCGAC
GTGCCCTTCCCCTTCTCCGCACAGTCCGGCGCCGGCGTGCCTGGCTGGGGCA
TCGCCCTGCTCGTGTTGGTGTGCGTGCTCGTGGCCCTCGCCATCGTGTACCTG
ATCGCCCTGGCCGTCTGTCAGTGCAGGAGAAAGAACTATGGGCAGTTGGATAT
CTTCCCCGCCAGGGACACCTACCACCCCATGTCCGAGTACCCCACCTACCACA
CCCACGGCCGCTATGTCCCTCCCTCCTCGACCGACCGCTCCCCTTACGAGAAG
GTGAGCGCCGGCAACGGAGGCAGCTCCCTGTCCTACACCAACCCTGCCGTGG
CCGCCACAAGCGCCAACCTGTCTAGA**TGA**CTCGAG

Figure 6 – Comparison of expression of native MUC1 (JNW656) and codon modified MUC1 (JNW758) following transient transfection into CHO cells.

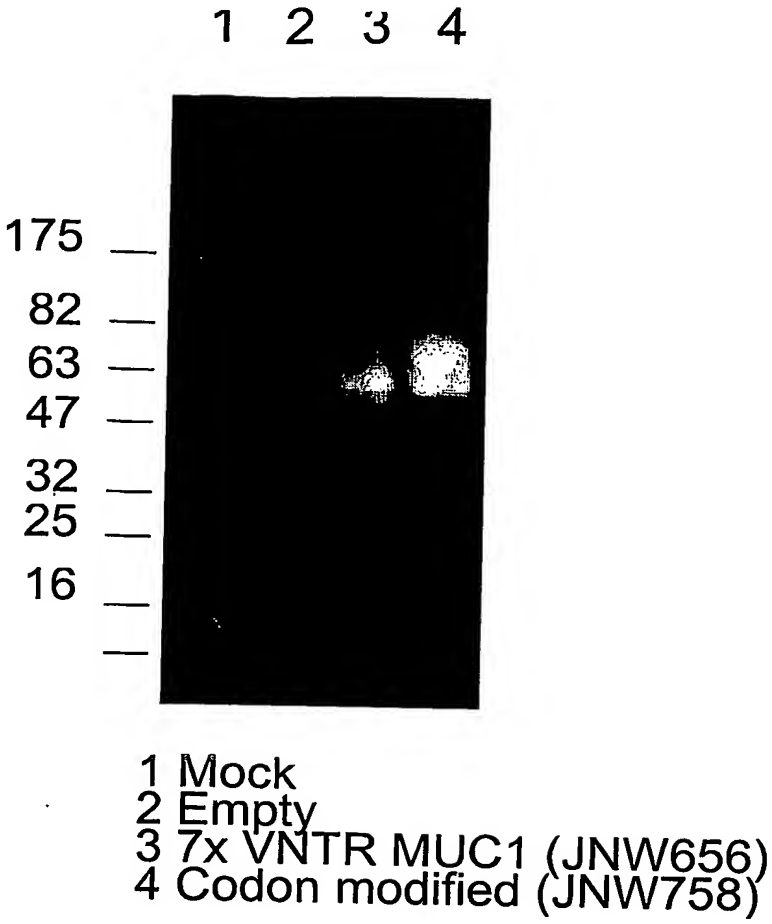


Figure 7 – Comparison of the IFNγ ELISPOT cellular responses following PMID immunisation with pVAC empty (control), 7x VNTR MUC1 (JNW656) and codon modified 7x VNTR MUC1 (JNW758). SAP is the CD8 MUC1 epitope SAPDNRPAL. Each bar represents an individual mouse.

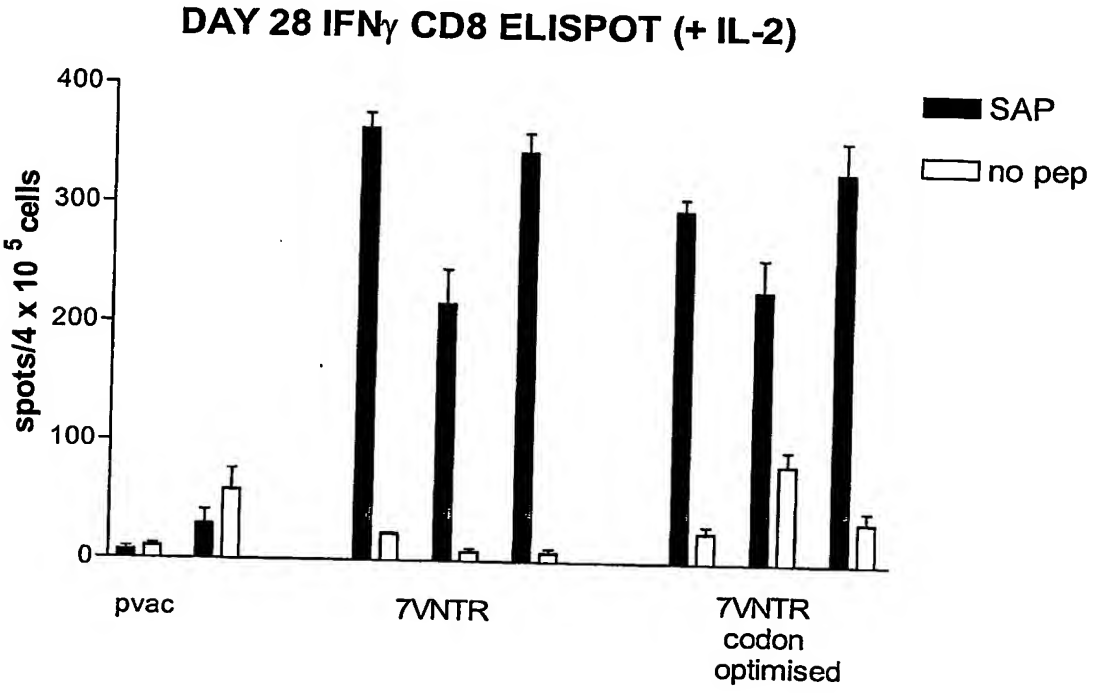
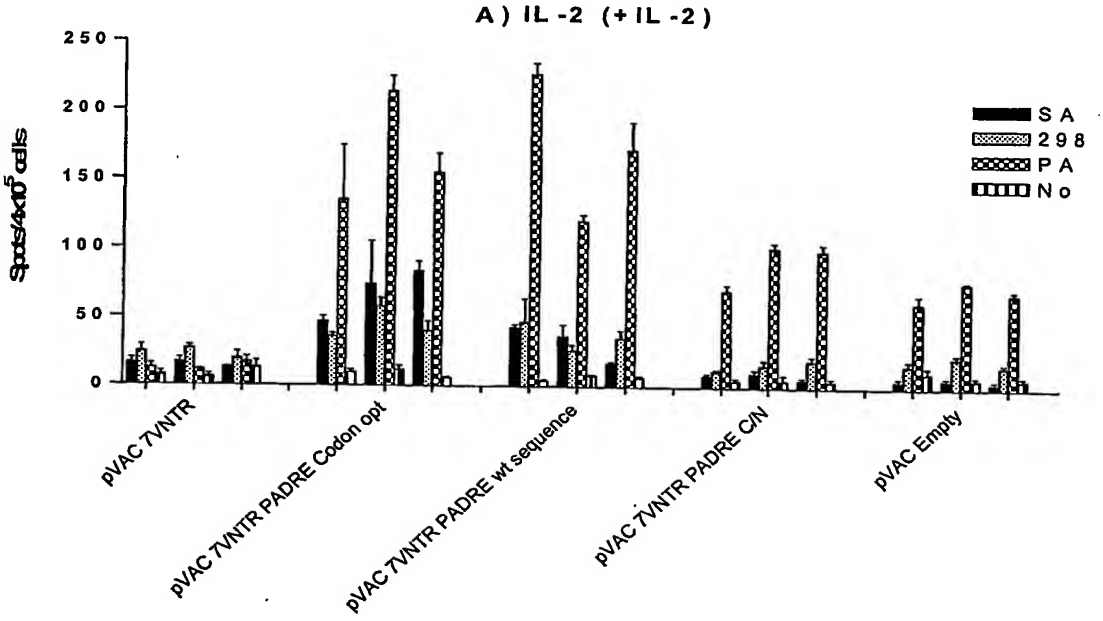


Fig 8. Comparison of the IL-2 ELISPOT cellular responses following PMID immunisation with PVAC 7 VNTR, PVAC 7 VNTR-PADRE-C (codon optimised sequence) , PVAC 7 VNTR-PADRE-C (wt sequence), PVAC 7 VNTR-PADRE C/N' (codon optimised sequence) and PVAC empty (control). Responses were read using SAP (CD8 T cell MUC1 peptide), 298/9 (CD4 T cell MUC1 peptide) and PADRE peptide. Analysis was performed at day 28 (A) and 49 (B).



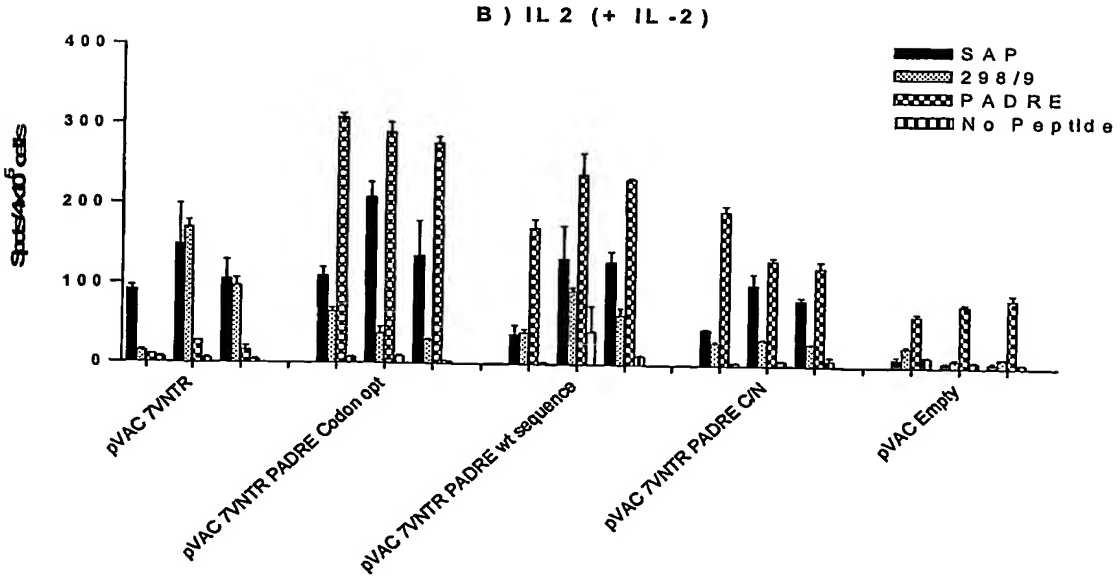


Figure 9

7x VNTR MUC1 (plasmid JNW656)

Protein sequence

MSRTPGTQSPFFLLLLLTVLTVVTGSGHASSTPGGEKETSATQRSSVPSSTEKN
AVSMTSSVLSSHSPGSGSSTTQGQDVTLAPATEPASGSAATWGQDVTSVPVT
RPALGSTTPPAHDVTSAPDNKPAPGSTAPPAHGVTSAPDTRPAPGSTAPPAHG
VTSAPDTRPAPGSTAPPAHGVTSAPDTRPAPGSTAPPAHGVTSAPDTRPAPGS
TAPPAHGVTSAPDTRPAPGSTAPAAHGVTSAPDTRPAPGSTAPQAHGVTSAPD
TRPAPGSTAPPAHGVTSAPDNRPALGSTAPPVHNVTSASGSASGSASTLVHNG
TSARATTTPASKSTPFSIPSHHSDTPTTLASHSTKTDASSTHHSTVPPLTSSNHS
TSPQLSTGVSFFFLSFHISNLQFNSSLEDPSTDYYQELQRDISEMFLQIYKQGGF
LGLSNIKFRPGSVVVQLTLAFREGTINVHDVETQFNQYKTEAASRYNLTISDVS
VSDVPFPFSAQSGAGVPGWGIALLVLVCVLVALAIVYLIALAVCQCRRKNYG
QLDIFPARDTYHPMSEYPTYHTHGRYVPPSSTDRSPYEKVSAGNGGSSLSYTN
PAVAATSANLSR.

DNA sequence

ATGTCTAGAACACCGGGCACCCAGTCTCCTTTCTTCCTGCTGCTGCTCCTCACAGTGCTTACAGTTGTTACAGGTTCTGG
TCATGCAAGCTCTACCCCAGGTGGAGAAAAGGAGACTTCGGCTACCCAGAGAAGTTCAGTGCCCAGCTCTACTGAGAAGA
ATGCTGTGAGTATGACCAGCAGCGTACTCTCCAGCCACAGcCCCGGTTCAGGCTCCTCCACCACTCAGGGACAGGATGTC
ACTCTGGCCCCGGCCACGGAACCAGCTTCAGGTTCAGCTGCCACCTGGGGACAGGATGTCACCTCGGTCCCAGTCACCAG
GCCAGCCCTGGGCTCCACCACCCCGCCAGCCCACGATGTCACCTCAGCCCCGGACAACAAGCCAGCCCCGGGCTCCACCG
CCCCCCCAGCCCACGGTGTCACCTCGGCCCCGGACACCAGGCCGGCCCCGGGCTCCACCGCCCCCCCAGCCCACGGTGTC
ACCTCGGCCCCGGACACCAGGCCGGCCCCGGGCTCCACCGCCCCCCCAGCCCACGGTGTCACCTCGGCCCCGGACACCAG
GCCGGCCCCGGGCTCCACCGCCCCCCCAGCCCACGGTGTCACCTCGGCCCCGGACACCAGGCCCGCCCCGGGCTCCACCG
CCCCCCCAGCCCACGGTGTCACCTCGGCCCCGGACACCAGGCCCGCCCCGGGCTCCACCGCGCCCCGCAGCCCACGGTGTC
ACCTCGGCCCCGGACACCAGGCCGGCCCCGGGCTCCACCGCCCCCCCAAGCCCACGGTGTCACCTCGGCCCCGGACACCAG
GCCGGCCCCGGGCTCCACCGCCCCCCCAGCCCATGGTGTCACCTCGGCCCCGGACAACAGGCCCGCCTTGGGCTCCACCG
CCCCTCCAGTCCACAATGTCACCTCGGCCTCAGGCTCTGCATCAGGCTCAGCTTCTACTCTGGTGCACAACGGCACCTCT
GCCAGGGCTACCACAACCCCAGCCAGCAAGAGCACTCCATTCTCAATTCCCAGCCACCACTCTGATACTCCTACCACCCT
TGCCAGCCATAGCACCAAGACTGATGCCAGTAGCACTCACCATAGCACGGTACCTCCTCTCACCTCCTCCAATCACAGCA
CTTCTCCCCAGTTGTCTACTGGGGTCTCTTTCTTTTTCCTGTCTTTTCACATTTCAAACCTCCAGTTTAATTCCTCTCTG
GAAGATCCCAGCACCGACTACTACCAAGAGCTGCAGAGAGACATTTCTGAAATGTTTTTTGCAGATTTATAAACAAGGGGG
TTTTCTGGGCCTCTCCAATATTAAGTTCAGGCCAGGATCTGTGGTGGTACAATTGACTCTGGCCTTCCGAGAAGGTACCA
TCAATGTCCACGACGTGGAGACACAGTTCAATCAGTATAAAACGGAAGCAGCCTCTCGATATAACCTGACGATCTCAGAC
GTCAGCGTGAGTGATGTGCCATTTCCTTTCTCTGCCCAGTCTGGGGCTGGGGTGCCAGGCTGGGGCATCGCGCTGCTGGT
GCTGGTCTGTGTTCTGGTTGCGCTGGCCATTGTCTATCTCATTGCCTTGGCTGTCTGTCAGTGCCGCCGAAAGAACTACG
GGCAGCTGGACATCTTTCCAGCCCGGGATACCTACCATCCTATGAGCGAGTACCCCACCTACCACACCCATGGGCGCTAT

GTGCCCCCTAGCAGTACCGATCGTAGCCCCTATGAGAAGGTTTCTGCAGGTAATGGTGGCAGCAGCCTCTCTTACACAAA
CCCAGCAGTGGCAGCCACTTCTGCCAACTTGTCTAGATAG